1227 25th Street, NW
Washington, D.C. 20037-1156

January 2, 2008

VIA ELECTRONIC MAIL

Thinh X. Nguyen
U.S. Food and Drug Administration
Office of Combination Products
15800 Crabbs Branch Way (HFG-3)
Suite 200
Rockville, MD 20855

Re: Introduction to the Combination Products Coalition

Dear Mr. Nguyen:

The Combination Products Coalition ("CPC") would like to offer its congratulations on your appointment as the Director of the Office of Combination Products ("OCP"). We wanted to take a moment to welcome you and to introduce you to our organization. We have enjoyed working collaboratively with the OCP over the past few years, and we look forward to further collaboration under your leadership.

I. BACKGROUND ON THE CPC

The CPC is a group of leading drug, biological product, and medical device manufacturers with substantial experience and interest in the combination products area. Our members are extraordinarily diverse, ranging in size from start-ups to multi-billion dollar manufacturers. Because of this diverse, cross-industry membership, we think the CPC brings a broad and unique perspective to issues affecting combination products.

All of our members share an intense interest in policy issues affecting combination products, and one of our principal goals is to work with FDA on such issues in order to advance our common mission of providing the best possible health care for patients. In this regard, the CPC has had frequent dialogue with the OCP on regulations, guidance documents, and other policy issues that affect combination products and how best to serve patient needs with respect to such products. For example, we have submitted dozens of written comments, policy documents, proposed guidance documents, and other materials to

the agency on these issues over the last four years. If you're interested, you can find several of these materials on our website: http://www.combinationproducts.com/.

In addition to the written materials, we have been heavily involved in sponsoring and facilitating discussions among industry and FDA with respect to combination products. For example, about two years ago, we worked very closely with the Regulatory Affairs Professionals Society ("RAPS") in organizing and sponsoring a two-day summit on regulatory issues involving combination products. We largely handled the content development for the meeting, drafted straw man position papers to frame the discussions, and organized the presentations. Over 150 professionals representing a wide range of research and academic institutions, industry, government, and trade associations attended this summit, and the meeting produced a white paper that the group submitted to FDA. As another example, several of our members participated in panels at the 2005 FDA/DIA Workshop on Combination Products and Mutually Conforming Labeling.

Throughout these exchanges, the OCP has been extremely patient-focused, helpful, and collaborative. We strongly believe that the OCP's approach to policy development in the combination product area has served patients, the agency, and industry well, and we look forward to continuing our dialogue with the OCP.

II. CURRENT KEY POLICY CONCERNS

We would also like to take this opportunity to describe our current chief concern with respect to combination products. In sum, we are very interested in seeing a proposed rule published on cGMP requirements for combination products, or, in the alternative, beginning a dialogue on that topic.

By way of background, in the spring of 2006, the OCP announced its intention to propose regulations for cGMPs for combination products.[1] The proposed rule was expected to be published in the first quarter of 2007. As of today, the rule has yet to be published, although we understand it is proceeding through the required internal sign-off process. The most recent projection for publication of the rule is May 2008.[2]

Before the agency announced its intention to publish a proposed rule, industry and OCP's practice was to work out cGMP issues quite collaboratively -- manufacturers would come to OCP with thorny cGMP questions, and the two would work the issues out together. This flexible and interactive process provided both FDA and industry with clarity and certainty regarding how cGMPs applied to specific combination products. Unfortunately, after FDA announced its intent to publish regulations, the OCP has been uncomfortable discussing the application of cGMPs to specific combination products.

---

[1] *See* Unified Agenda of Federal Regulatory and Deregulatory Actions Spring 2006, available at: http://www.fda.gov/oc/industry/unifiedagenda/spring2006.html.

[2] *See* Unified Agenda of Federal Regulatory and Deregulatory Actions Fall 2007, at: http://www.reginfo.gov/public/do/eAgendaViewRule?ruleID=279345.

This state of limbo has left manufacturers in a bind, particularly manufacturers that are at the pivotal stage of moving from the design phases to production and are therefore building production facilities. These manufacturers need further clarity, which the OCP is not currently giving. At the same time, to give patients access to innovative products, manufacturers must move forward even without much-needed clarity on quality controls. This current lack of transparency is especially taxing for small or start-up companies. And it has gone on now for almost two years.

Quite simply, the need for clarity and transparency on cGMPs is critical. We believe that the agency should either publish the proposed rule promptly, or allow industry to resume their former dialogue with OCP.[3]

III. ANTICIPATED FUTURE COLLABORATION WITH OCP

In reviewing our past work, we found that we have analyzed and submitted materials to OCP on nearly every issue impacting combination products, including cGMPs, cross-labeling, adverse event reporting, submissions, post-approval modifications, and more. In this letter, we want to describe two current projects about which we're particularly excited.

First, we very recently completed a survey on the need for FDA guidance on issues impacting combination products. We have attached a Microsoft Word version of the survey to this e-mail. The survey is designed to assess whether guidance is needed, and, if so, what form such guidance might take (e.g., FAQ/Q&A, traditional guidance document, etc). Over the past few months, we have worked with several trade organizations and industry publications to publicize and disseminate this survey as widely as possible throughout the combination product industry, and we are currently in the early stages of analyzing the results. After we finish our analysis, we would like to meet with you and your team to present and discuss the results and how they might impact our agendas for combination product policy development. We are tremendously excited about this survey because to our knowledge, this information has not been collected in a systemic and comprehensive manner. We truly think the results will be invaluable in setting our agenda for 2008 and beyond.

---

[3] We recognize that the agency is not permitted to tell people what is going to be in a proposed rule before it comes out. However, the APA does not prohibit contact between members of the public and the agency concerning a rule that is being developed through notice and comment rulemaking. While formal rulemaking does prohibit certain forms of contact, notice and comment (i.e. informal) rulemaking includes no such restriction. We also recognize that, in the past, a few courts have found bias in a rulemaking when there is too much one-on-one contact between certain members of the public and the agency officials developing a proposed rule. In those cases, they have invalidated the rule on the grounds that it is based on evidence not in the administrative record. The solution to this problem, though, is for the agency to make sure that the substance of conversations about a proposed rule ends up in the record, which is required by FDA regulations anyway. *See* 21 CFR §§ 10.40(f)(1), 10.65. (By the way, wearing an American Bar Association hat, I am planning a meeting with the FDA Office of Chief Counsel to clarify the rules on the agency not talking during certain phases of rulemaking and guidance development.)

Second, we have been working with OCP and RAPS to plan a conference on the cGMP proposed rule that would take place ideally within the comment period. Our plan for the conference is as follows: First, we envision the conference as having FDA speakers talk first to describe the contents of the proposed rule. Second, we are planning to have breakout sessions in which small groups of participants apply the proposed rule to case studies that we have already drafted. Third and finally, we would like for a representative from each group to present issues they identified in applying the proposed rule to the case study. We realize that scheduling the conference within the rule's comment period will require us to act very fast, so we have already begun the preparation. We are happy to send you the case studies if you would like. We have already shared them with Jim Cohen.

We're looking forward to continuing our work on the guidance survey and the meeting on the cGMP regulations, and we welcome the opportunity to discuss these projects, or any of our other past or current work, with you.

IV. CONCLUSION

In conclusion, we would like to extend an offer to work collaboratively on combination product issues with you and your team. While we have shared some of our thoughts and experience in this letter, we would love to hear your ideas. After you get settled, perhaps I can give you a call to discuss. Hopefully Jim Cohen and Patricia Love can vouch for our willingness to be helpful and supportive in the policy development that is most important to the OCP.

If we can help in any way, please do not hesitate to contact us. You can reach me at (317) 514-5008 or at bthompson@ebglaw.com. We look forward to continuing our relationship with the OCP.

Kindest regards,

Bradley Merrill Thompson,
On behalf of the Combination Products Coalition